



# **Europe is Won Before Launch**

## **The Leadership, Access and Evidence Playbook for Rare Disease Biotech**

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# The European Rare Disease Equation: Access, Evidence and the Leaders Who Can Solve It

Rare diseases collectively affect an estimated 36 million people across Europe, representing one of the largest areas of unmet medical need despite major advances in precision medicine, genomics and targeted therapeutics. (1,2) While more than 6,000 rare diseases have been identified globally, only a minority currently have approved treatment options available to patients. (1) Over the past two decades,



European orphan medicine frameworks and scientific innovation have transformed the landscape, stimulating investment and accelerating development pathways.

## Key Challenges in European Rare Disease Access



Delayed  
Diagnosis



Regulatory  
Complexity



HTA  
Assessments



Pricing  
Negotiations



Reimbursement  
Delays



Equitable Patient  
access across  
European  
markets (1,3)

Against this backdrop, rare diseases have evolved from a niche therapeutic area into a strategic growth driver across global biopharma. Recent Q1 financial results and strategic announcements from major organisations reinforce this momentum:

- AstraZeneca reported continued growth within its Rare Disease portfolio, generating approximately \$2.4 billion in Q1 2026 revenues, while companies including Ipsen, Sanofi, BioMarin, Vertex, Novartis, Sobi and UCB continue expanding investments in specialty medicines and genetically targeted therapies. (4–9)
- Recent corporate activity reinforces the same trend. Angelini's \$4.1bn acquisition of Catalyst, Chiesi's \$1.9bn KalVista deal, Alfasigma's rare-disease and specialty-care investments, and Recordati's renewed private-equity-backed strategic focus all point to a market where scientific innovation, international scale and launch excellence are becoming decisive. (10–13)

**However, scientific innovation alone does not guarantee successful commercialisation. Launching rare disease products in Europe increasingly requires sophisticated approaches to evidence generation, market access strategy, country prioritisation, organisational design, patient identification, and talent capability building.**

This whitepaper draws upon public market data alongside insights collected through discussions with general managers and senior commercial, medical and access leaders across Europe to explore the current rare disease launch environment.

Taken together, these observations show that rare disease and specialty assets are core growth engines at major large and mid-cap European pharma companies, and that capital is being deployed aggressively into rare disease pipelines and platforms at multibillion or high nine figure scales. They also show that European and global Q1 performance is sensitive to launch trajectories, patient switches and reimbursement timing in rare disease.

At the same time, the European path to market has become more volatile and fundamentally driven by pricing and market access. Rare disease leaders across oncology, neurology, metabolic and endocrine conditions converge on one point: the bottleneck is no longer "can we sell?" but "can we secure and sustain funded access on viable terms over multiple years?"

## Pricing and HTA dominate launch complexity



Pricing, HTA and access now drive roughly a third of rare disease launch complexity in Europe, more than any other single factor. The core issue is that Europe is not a single market: 27 EU member states plus the UK, Switzerland, Norway, and others each have their own HTA bodies, evidentiary standards, and pricing rules.

A single global value dossier rarely passes; companies must localise comparators, endpoints, subgroup and RWE strategy, and budget impact models country by country.

On top of this, external reference pricing and parallel trade mean that an early low price or heavy discounting in one market can cascade across Europe, forcing manufacturers into difficult sequencing decisions: where to launch first, at what list price, and with which confidential rebates to protect long-term net price integrity.

In addition, commercial leaders observe that boards and executives face an early, often underestimated strategic trade-off: over a horizon of five to seven years, should they prioritise (i) the highest possible cumulative sales through speed of access and broad uptake, or (ii) the highest possible confidential net prices and tight control of discounting?

**In most European markets, It is extremely difficult to maximise both simultaneously. Decisions on list price, discount depth and launch sequencing effectively “lock in” one direction or the other.**

Our discussions have highlighted a key point: many non European organisations also underestimate how list and net pricing work in Europe. In most markets, you can set a relatively high public list price because payers really negotiate on the confidential net price.

The list price mainly matters for external reference pricing, while the true price is hidden in rebates, managed entry agreements & clawbacks. This allows companies to keep a strong list price for reference, while quietly managing budget impact & international reference risk through confidential discount

In this environment, complexity for general managers (GMs) has become shorthand for cost-effectiveness thresholds, comparators and budget impact. In the UK, for example, NICE acts as a binary gatekeeper.

A single negative appraisal in a rare disease can trigger a full commercial reset, initial buildup of a launch team, rapid downsizing, and then selective reinvestment while a second appraisal, often three to six months away, is pursued. Affiliates operate for prolonged periods as “all loss, no profit,” funding market access work and maintaining a minimal footprint during appraisal cycles.

Even where reimbursement is achieved, some systems anchor assessments against ultracheap generics, leaving little room for high-end rare disease pricing. Smaller “premium” markets can prove slower and more rigid than expected. Against this backdrop, uptake depends not only on HTA success but also on patient finding and local implementation. The net result is that pricing and HTA determine where and when companies can play; access strategy, stakeholder alignment and patient finding determine whether they can actually win.

### **Evidence generation: comparators, endpoints, orphan status and RWE**

US development and approval pathways for rare diseases rarely translate directly into European success.

Many US approvals are secured via accelerated routes on biomarker or surrogate endpoints, an approach that can work well with the FDA, but EMA and national HTA bodies are far less willing to accept early surrogate data without clear translation into patient relevant outcomes and a robust value story.

One international head who obtained US-accelerated approval based on biomarkers states that this approach works in the US but does not translate directly to Europe, where companies need an additional, more clinically oriented study. This typically means an added two to three years before meaningful European access is possible.

**Across the leaders we spoke with, there is broad consensus that any global value dossier intended for Europe must, at minimum, do five things well:**



**Comparator choice:** Select and justify a comparator that reflects true standard of care in the target countries, not just a convenient control arm for registration. This is repeatedly cited as the single most underestimated factor in European access. Payers and HTA bodies will ask "What are you comparing against?" before almost any other question; a lack of direct or credible indirect comparison to standard of care is a major handicap.



**Hard clinical endpoints:** Whenever feasible, demonstrate impact on hard outcomes like survival, organ preservation, irreversible morbidity, rather than relying solely on surrogate markers or composite scores.



**Orphan status and regulatory advantages:** Orphan designation, where applicable, can support more favourable benefit assessments and extended market protection periods in many European countries. While this is well known to regulatory teams, commercial and access leaders emphasise its practical downstream impact on pricing corridors and negotiation leverage.



**Maintaining access through post launch RWE agreements:** Several affiliates have managed to secure or keep reimbursement by promising to run structured real world evidence (RWE) studies after the price is agreed. For example, in one country, payers were about to remove price and reimbursement for part of the patient population, but they accepted a deal instead: the company would collect and submit RWE over two to three years, and in return the payer kept reimbursement in place for those patients while the new data were generated.



**Budget impact across scenarios:** Robust models should present multiple budget impact scenarios (e.g. treating only the most severe patients as opposed to broader populations), effectively giving payers a set of choices rather than a single "take it or leave it" proposal. This allows alignment between clinical need, affordability and political acceptability.

European decision makers now expect longer term outcomes, strong comparators and indirect treatment comparisons, plus a value narrative that convinces both regulators and payers.

Where data are **“pretty robust but not the most robust,”** gaps in comparator evidence, immature follow up, or unpublished analyses quickly become material weaknesses that drive re submissions or outright rejections.

Some US biotechs underestimate how different these processes are compared to how things work stateside, as well as how much organisational build they requires. Many arrive with R&D heavy, commercially light structures, missing key functions such as medical affairs and central market access.

The result is that US firms must build their European operations from scratch, frequently relying on a single senior hire, often starting with essentially zero market knowledge, who must design systems, supply chain, regulatory and access capabilities across Europe and other regions.

Macro and financial constraints, including USD/EUR FX swings and constrained healthcare budgets, further compress margins and narrow the room for error.

For biotechs moving from R&D to commercial, the implication is clear: success in Europe is not merely about having a strong product and non-European demand, but depends on rethinking evidence generation, value communication, and organisational design specifically for the European market. Innovative access models, including subscription arrangements (“pay X per year, treat as many as you want”) and risk sharing agreements with outcomes based refunds for non responders, are becoming more common.

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Particularly in rare diseases with high per patient costs. From a pricing architecture perspective, these models have an additional benefit: they can make the true net price less transparent to external observers, since the effective price per treated patient depends on volume and outcomes over time rather than a simple unit price. For companies concerned about international reference pricing and MFN dynamics, this opacity can be strategically valuable.

## Early access programmes and pre launch engagement

One of the most frequently overlooked levers by non-European companies is the role of early access programmes (EAPs) or analogous schemes. Experienced leaders describe EAPs as “fundamental” to later price and reimbursement outcomes.

In several markets, payers directly fund early access, meaning that companies can begin treating patients and generating experience before formal reimbursement while still covering or even exceeding local operating costs.

There are documented examples where affiliates achieved profitability in year two purely based on paid early access programmes, long before full commercial launch.

### Certain Countries, Including

**France, Greece and Portugal**, are cited as markets where well designed EAPs have created substantial early revenue streams.

### Beyond Economics, Early Access Provides Three Strategic Benefits:



**KOL and guideline support:** Running EAPs, often linked to local clinical studies, helps build relationships with key opinion leaders and supports inclusion in treatment guidelines.



**Patient and advocacy mobilisation:** Patient organisations in rare disease often play a visible role in access debates. Early access, coupled with transparent communication, can create strong patient advocacy for funding when HTA decisions are pending or contested.



**Real world data:** Structured EAPs can be a powerful source of real world evidence on treatment patterns, adherence and outcomes, feeding back into HTA submissions, reassessments and post launch optimisation.

Taken together, these factors mean that in many European countries, arriving at price and reimbursement discussions without a history of early access is a significant handicap, not just a missed opportunity.

## Lean Teams, Outsized Responsibilities

Rare disease and specialty leaders in Europe typically run lean teams with outsized responsibilities yet are still expected to deliver big pharma level outcomes.

**In many cases, the GM is effectively employee number one, simultaneously setting up the**



Some GMs spend a small portion of their time on their formal job description and in most cases, leaders arrive to find essentially nothing in place outside the US. As such, they also must construct early-access frameworks, regulatory dossiers and commercial operations.

Affiliates often consist of small lean teams, but still have to navigate the NHS, NICE and regional payers, engage clinicians, and execute several oncology or specialty launches in parallel. Internally, the GM must orchestrate market access (often part of a global team), local medical affairs (dual reporting to the GM and global functions) and nascent commercial roles. Externally, they must coordinate a dynamic ecosystem of patient groups, expert centres and KOLs, often in fast moving areas like CNS or oncology.

Our observations is that in smaller affiliates, mis-hiring is disproportionately damaging compared to a larger pharma organisation, making talent selection, role design and cross functional alignment critical to success.

## What the launch playbook looks like

### Market sequencing and model

Germany remains the anchor market in Europe, with the UK, France, Italy and Spain still representing most of the revenue opportunity. Experienced European leaders increasingly segment markets into three broad “buckets” from an access perspective:

#### **Bucket 1 The free pricing, rapid access:**

Germany and Luxembourg, where list prices can initially be set freely and access is relatively fast, albeit followed by rigorous negotiations and, in Germany, AMNOG assessments.

#### **Bucket 2 The clinical assessment with budget negotiations**

Countries such as Italy, Spain, France, Austria, Switzerland and, in some cases, Greece, where access hinges on a clinical assessment or benefit rating which then serves as the starting point for intensive price and budget impact negotiations. The assessment opens the door, but the final terms depend on negotiation skill & flexibility on both sides.

#### **Bucket 3 The HTA driven price setting**

The UK, the Netherlands, Portugal, Belgium and the Nordic countries, where formal HTA and health economic models largely determine the reimbursed price. While there can be some room for manoeuvre, these systems are less open to purely negotiation driven uplifts.

This segmentation has practical consequences for launch sequencing, resource allocation and evidence planning.

**For instance, products heavily dependent on favourable cost effectiveness ratios may face structurally tougher conditions in Bucket 3 countries than in those where clinical assessment and negotiation carry more weight.**

## Organisation design: minimum viable affiliate

Headcount is stage gated to HTA and first reimbursement, with early builds focused on a small, senior core (GM, market access, medical, finance/operations) and heavy use of outsourcing/virtual setups. Field forces come last, often staying in the single digit/low teens FTE range even at maturity, while large legacy affiliates are being reshaped from sales driven to medical and access led. The guiding principle is a **“minimum viable organisation”**: enough capability to secure access and early use without locking in fixed costs.

Leaders with repeated build experience emphasise that in key markets, a minimum of three to five in country FTEs is typically required 12–24 months before launch to execute critical tasks:



Attempting to parachute in a launch team only shortly before price negotiations, without prior clinical or advocacy groundwork, is repeatedly cited as a common but avoidable mistake.

In **Germany, Italy** and **Spain** in particular, “scaling for access” also means planning for regional as well as national negotiations. After securing a national decision, companies often face a second wave of discussions with regional authorities, hospital consortia or payer bodies, a dynamic that seasoned leaders liken to negotiating with US pharmacy benefit managers (PBMs). Ignoring this regional layer can delay real world uptake long after formal reimbursement is obtained.

Finally, companies must plan early for legal entity creation and distribution set up. Each target market requires its own legal entity and localisation work (including country specific blue box labelling and local GxP frameworks for pharmacovigilance, quality, regulatory, medical information and product complaints). This cannot be done in one month from a single pan European hub. While some functions can be centralised or outsourced, there must be a coherent design and oversight model in place well ahead of launch.

## Europe–HQ alignment and leadership complexity

European GMs now see bringing US headquarters up to speed as a core part of their role. Boards are briefed specifically on European regulatory and HTA risk. This increasingly includes explaining that Europe is not only a compliance and access challenge, but also a strategic opportunity for new entrants from outside the traditional US-EU axis, including Asian biopharma companies building their first European footprint.



**Our observation is that leaders who succeed in this environment typically combine:**



### **Big pharma and biotech/scale-up experience**

They have run sizeable P&Ls but also been “employee number one” in lean builds, thus knowing what “good” looks like while coping without big company infrastructure.



### **A cross functional, non-siloed mindset**

They move naturally across medical, market access, commercial and operations, leading integrated HTA strategies and building cultures around shared outcomes.



### **Resilience and intrinsic motivation**

They are not afraid to roll up their sleeves through HTA reversals, policy shifts and hiring freezes, such leaders motivated by more than title and pay.

**Our market feedback suggests that the first critical hires are consistent:**

- GM or commercial leader, market access and medical affairs as non-negotiable core;
- Finance/operations or a Head of Office for backbone and compliance;
- Commercial field roles typically come later; these are sometimes outsourced and/or hybrid at first;

While there is a broad pool of experienced pharma executives, companies report a shortage of leaders who have experienced the full rare disease cycle in Europe (positive and negative HTA, build up & downsizing). Identifying those profiles, and stress testing for resilience and cross functionality, is now critical.

## Choosing where to base the European HQ is another area where seasoned leaders counsel deliberate trade-offs. Five factors recur in their thinking:

- 01 Tax efficiency (e.g. Ireland, the Netherlands, Switzerland, Portugal) and overall fiscal stability
- 02 Depth of talent pools in key hubs (e.g. Zurich/Zug/Basel, Munich, Frankfurt)
- 03 Need for strong local presence and language expertise in major markets
- 04 Potential benefits of locating manufacturing or R&D in specific countries to support access and political goodwill
- 05 Regulatory and logistical implications of legal entity structures across multiple countries.

Some companies choose HQ locations primarily for tax or talent reasons; others prioritise proximity to their largest markets.

Leaders stress less the "right" answer than the importance of knowing why a given location is chosen, and aligning legal and operational structures to that choice from the outset.

## Based on our understanding on the market, the message for boards and global executives is:



Treat **Europe** as a long term investment, with multiyear "all L, no P" phases and binary HTA risk.

Put pricing and HTA at the centre of early decisions.

Involve **European access leaders** in Phase II/III design and comparator/RWE choices.

Back and **listen to your European GM**, giving them a real voice on strategy, sequencing and resourcing.

**On the other side, based on what we have seen and heard, the incoming Heads of Europe/GMs should:**

Do hard due diligence on assets, access risk and HQ mindset;

Start with a small, high impact core and avoid overbuilding before proof points;

Invest early in cross functional ways of working and peer networks;

Prioritise early access, guideline/KOL engagement and patient advocacy as core launch enablers, not "nice to have" add ons once HTA is complete.

Launching rare disease therapies in Europe is a test of access strategy, evidence design and leadership quality more than field force scale.

The winners will be those who confront complexity early, design lean but resilient organisations, and back the few leaders capable of solving the European rare disease equation.

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